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Is hospital admission valuable in managing syncope? Results from the STePS study

Giorgio Costantino[1], Franca Dipaola[2], Monica Solbiati[1], Mara Bulgheroni[2], Franca Barbic[2], Raffaello Furlan[2]

[1]Medicina ad Indirizzo Fisiopatologico, Dipartimento di Scienze Biomediche e Cliniche "L. Sacco", Ospedale "L. Sacco", University of Milan, Milan, Italy
[2]Internal Medicine, Department of Medical Biotechnologies and Translational Medicine, Humanitas Clinical and Research Center, Rozzano, University of Milan, Milan, Italy

Abstract

The proper way to test the usefulness of hospitalization in syncope patients would be to conduct a randomized controlled trial. However, this approach is characterized by major theoretical and ethical limitations which make this procedure unfeasible. Data from observational studies indirectly show that hospitalization might help reduce the short-term risk of death and adverse events by promptly identifying and treating life-threatening events or conditions. Future research should focus on identifying which patients will benefit from hospitalization. In this regard, we should be able both to correctly risk-stratify patients and to analyze syncope observation units and protocols, which may provide a safe alternative for the evaluation of intermediate--risk patients. (Cardiol J 2014; 21, 6: 606–610)

Key words: syncope, hospitalization, observation units, risk stratification

Introduction

Two patients presented to the Emergency Department (ED) with syncope.

The first was a 72-year-old man, complaining of syncope without prodromes. He had had 2 syncope episodes in the last week. The first one happened while he was standing at the supermarket. The second episode occurred while he was walking and resulted in head trauma. Head computed tomography scan was unremarkable; his electrocardiogram (ECG) showed a previously known left bundle branch block. The medical history was consistent with a previous (5 years before) myocardial infarction with preserved ejection fraction. His medical therapy included angiotensin-converting enzyme inhibitor, beta-blocker, aspirin, statin.

The second patient was a 20-year-old woman who fainted while standing at a concert. Syncope was preceded by prodromes (blurred vision).

Which patient needed or would benefit from hospital admission?

In this paper, we will address the question whether hospitalization may reduce adverse events after syncope.

Effectiveness of hospital admission in syncope patients: Methodological considerations

From a methodological point of view, the best answer to the above question would be furnished by a randomized controlled trial (RCT). A hypothetical trial could be designed in two different ways:

Address for correspondence: Raffaello Furlan, M.D., Internal Medicine, Humanitas Clinical and Research Center, Via Manzoni, 56, 20089 Rozzano, Milan, Italy, tel: +39 028224 7228, fax: +39 028224 4590, e-mail: raffaello.furlan@humanitas.it
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1. All patients presenting with syncope to the ED could be randomized to hospital admission/ /discharge to assess hospitalization's impact on the outcome;
2. Only high and intermediate risk patients could be randomized in a similar trial.

In the first case, the young woman might be admitted, in contrast to the usual clinical practice and common sense. In the second case, we would decide *a priori* to exclude the young girl from randomization, however, are we sure that she would not gain any benefit from hospital admission? Moreover, in both cases, the man could be randomly put in the discharge arm of the trial. Do we think that such an approach would be ethical?

In 2003, Gordon Smith and Jill Pell published a systematic review in BMJ [1] concerning the potential use of parachute to prevent death and major trauma related to the gravitational challenge. They concluded that, similar to many interventions intended to prevent illness, so far the effectiveness of parachutes had not been subjected to rigorous evaluation by using randomized controlled trials. Since advocates for evidence based medicine have criticized the adoption of interventions evaluated by using only observational data, the authors suggested that they could organize and participate themselves in a double blind, randomized, placebo controlled, crossover parachute trial.

Among the dozens of letters to the Editor concerning this article, Victor Montori [2] reported that 2 friends of his had decided to conduct the RCT suggested by Smith and Pell [1]. The volunteer with the parachute survived, while the other person, randomized to parachute off, died due to the ground impact. The survivor was psychologically devastated (felt worse than being dead) and killed himself 3 months later. The author concluded that the 100% reduction in the risk of dying on impact is clearly valid and convincing. However, there was no difference in 3-month mortality between the two study arms. In addition, the quality of life seemed worse for the subject in the parachute arm of the study. Coming to the real purpose of the letter, Montori wanted to highlight that RCTs are useful only if there is equipoise between the two treatments. If good observational studies had already proven the utility of parachute, it would be unethical to do a RCT.

Evidences of effectiveness of hospital admission in syncope patients

If syncope etiology is identified during ED stay, the patient will be managed according to the underlying condition. For example, if pulmonary embolism (PE) is the cause of syncope, the patient will be admitted or discharged according to his PE risk profile [3] and syncope prognosis will be defined by the PE. Conversely, if a vasovagal cause of syncope is confirmed, the patient will be discharged unless his frailty or social condition requires an admission. The problem arises for those patients in whom a proper diagnosis cannot be provided in the ED. Notably, these patients represent up to 30–50% of ED syncope patients [4, 5]. Does hospitalization reduce the risk of adverse events in this population?

There is no direct answer to this question but indirect evidence can be obtained. A recent study reported that the risk of adverse events in admitted patients is fairly low [6]. However, others reported that the risk of adverse events in discharged patients is not negligible [7] and may be as high as 9.7% at 30 days. Considering all the prospective studies on syncope in the ED, the risk of 10-day adverse events is highly heterogeneous, spanning between 5% and 20% [8]. The 30-days risk of death was reported to be as high as 5% [9].

It is important to point out that hospitalization could be useful for three different reasons:

1. It may reduce the risk of death and adverse events in the short term. This is achieved by monitoring the patient, so that an adequate therapy can be promptly instituted in case of life-threatening events.
2. It may help to obtain an early diagnosis that could be otherwise impossible, thus potentially reducing adverse events in the long-term period.
3. It may allow treatments that cannot be done without hospital admission, such as pacemaker or implantable cardioverter-defibrillator (ICD) implantation.

Notably, the decision to admit a patient should also take into account the possible adverse events related to the hospitalization itself. Therefore, this risk should be smaller than the overall benefit gained by the diagnosis and therapy [10]. However, in spite of a number of clinical decision tools to assess the risk of adverse events [11–14], it is difficult to set up a decision threshold for hospitalization.

The Short-term Prognosis of Syncope (STePS) study [15] was specifically designed to test if hospitalization could be useful in patients with syncope. More than 650 patients were prospectively enrolled in 4 Italian EDs in 2004. The authors addressed the problem of the usefulness of hospital admission in patients with syncope by two different approaches.

1. First, they considered the number of major therapeutic procedures (namely pacemaker or ICD insertion, cardiopulmonary resuscitation, admission to intensive care unit, acute anti-arrhythmic therapy), hospital readmission for syncope and death in both admitted and discharged patients. They assumed that if one of these procedures had been done during hospitalization, then the hospital admission itself would have been useful. In addition, if the death rate had been similar between admitted and discharged patients then we could speculate if these procedures would have saved some lives. Indeed, while in the short-term period major therapeutic procedures were 14.7% and 2% in the admitted and discharged patients, respectively ($p < 0.01$), death rates were similar (1.4% vs. 0.4%, p = NS) in both populations. This suggests that major therapeutic procedures saved lives and that hospital admission was effective for those patients. However, it must be highlighted that, although the study was underpowered to detect death rate differences between the two groups, a 15% rate of major therapeutic procedures in the admitted patients suggests that the death rate could have been higher if these patients would have been discharged.
2. The second way to test whether or not hospitalization might be useful was to compare risk factors for short- and long-term outcomes and the long-term prognosis between admitted and discharged patients. Interestingly, the risk factors for short- and long-term outcomes differed. While short-term risk factors (abnormal ECG, trauma, absence of prodromes, male gender) were probably related to the severity of the syncopal episode, the risk factors for long-term outcomes (age > 65 years, neoplasms, cerebrovascular diseases, structural heart diseases, ventricular arrhythmia) seemed more related to the frailty of the patient. Indeed, the rate of adverse events at 1 year was higher in the admitted patients than in the discharged ones (Fig. 1). The same conclusion was also suggested by the EGSYS 2 follow-up study [16] and by Kapoor and Hanusa [17]. The latter was a prospective cohort study of patients with syncope matched to a group of patients without syncope according to age, gender, site of care (inpatient/ outpatient) and cardiac diseases. Patients with and without syncope had similar rates of cardiovascular outcomes, 1-year overall and cardiac mortality.

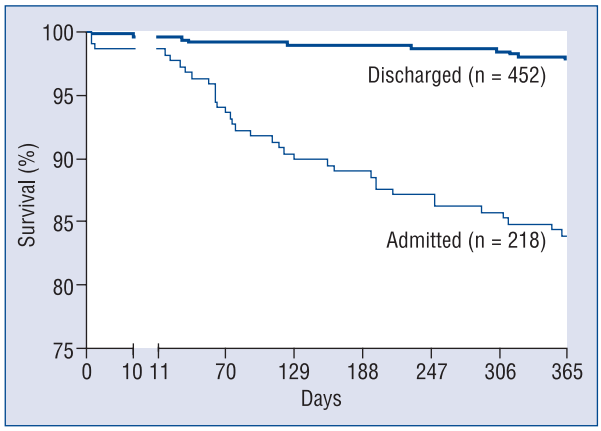

Figure 1. One year survival curves of admitted and discharged patients from the STePS study [15]. Notice that survival was significantly lower in admitted patients ($p < 0.0001$). This apparently confounding finding stems from the fact that admitted individuals were older and more sick.

Predictors of death were male gender, age > 55 years, and congestive heart failure, thus showing that underlying heart diseases and patient's vulnerability are risk factors for long-term mortality regardless of the presence of syncope.

In summary, since the syncope 30-day death rate is not negligible and might be prevented by some lifesaving procedures, we do believe that the question is no more if hospital admission is useful for syncope patients but in whom hospitalization can be effective.

The hospitalization rate vary largely worldwide, spanning between 10% and 90% [8, 9], and being about 35% in the STePS study.

The first international workshop on syncope risk stratification was held in Gargnano, Italy, in September 2013. Discussants from all over the world were asked to anonymously declare which rate of hospitalization they considered appropriate for patients with unexplained syncope. Most of the experts asserted that the appropriate admission rate would be less than 30%. Since about 50% of syncope patients receive a diagnosis in the ED [18], this means that the optimal rate of hospitalization should be around 15% of all patients who present to the ED because of syncope.

Thus, the correct approach for loss of consciousness management in the ED, after recognizing it as syncope, should be to focus on a correct etiopathogenetic diagnosis. If the diagnosis is reached, the patient will follow its management

strategy unless the presence of frailty or comorbidities requires a different approach. If syncope remains unexplained, a decision about admission or discharge is more complex and patients will need a proper risk stratification to recognize those who deserve hospital admission [19].

Currently, no prediction tool can replace an adequate clinical judgment about the decision whether to admit or discharge patients who are neither at high nor at low risk [8, 20, 21]. The most promising way to improve management strategies that could safely reduce hospitalization rates is probably the development of observation units and syncope unit protocols [19, 22]. Two randomized trials compared standard care and 6 h [23] or 12 h [24] structured ED-based observation protocols in intermediate risk patients. Results showed that ED syncope units/protocols can reduce hospitalizations, length of stay, and costs without apparent effect on serious clinical events, quality of life, and patient satisfaction. However, both studies enrolled a limited number of patients and additional work is needed to definitively demonstrate the safety and efficacy of such an approach.

Another important issue indirectly affecting the decision to hospitalize is to establish which is the most suitable ward to admit the patient. Since the aim of hospitalization is to early diagnose and treat life-threatening conditions (such as arrhythmias), syncope patients should be admitted in a continuous ECG-monitored bed.

Direction for future researches

The ideal way to test the usefulness of hospitalization in syncope patients would be to conduct a RCT, however this approach doesn't seem to be appropriate in this setting. Indeed, data from observational studies show that the rate of adverse events in non no-risk patients is too high to safely randomize them to discharge. However, data from observational studies indirectly show that hospitalization might help reduce the short-term risk of death and adverse events by promptly identifying and treating life-threatening events or conditions.

In our opinion, research must focus on identifying which patients will benefit from hospitalization, namely who will have more benefits (adverse events avoided, potential life-threatening diagnosis provided and useful treatments established) than harms from admission. To answer this question, we should be able to correctly risk-stratify patients. Identifying "no-risk" patients would be the best for emergency physicians. However, no-risk patients are likely to be young and healthy individuals who have a presumptive vasovagal mechanism; identification of such patients is unlikely to improve practice since they are almost never admitted. A true "zero risk" is probably impossible to reach in patients for whom there is currently uncertainty about clinical management. A more reasonable approach could be to find the way to assess patient's risk as a continuum, so that physicians working in different clinical settings can decide which threshold to adopt for admitting patients.

A second step will be to analyze syncope observation units and protocols, which may provide a safe alternative for the evaluation of intermediate--risk patients. In this regard, we believe that more evidence is needed. Since randomized evaluation of health services interventions may not be feasible, alternative evaluation designs might include randomized cluster trials, randomized registries, and evaluation of natural experiments (e.g., pre-post intervention with control) [19].

Conclusions

The proper way to address the problem of the effectiveness of hospital admission after syncope would be to do a RCT. However, this approach is characterized by major theoretical and ethical limitations which make this procedure unfeasible. Although indirect, there is enough evidence that hospital admission may be effective in some patients with syncope.

The main issue dealing with syncope in the ED is to identify the patient who needs hospitalization. The best strategy to manage these patients (observation unit, syncope unit, short admission, outpatient monitoring systems) is still under evaluation.

The worldwide rate of hospitalization for syncope is very heterogeneous and presently it is likely that an excessive number of patients with syncope are admitted to hospitals. Future research should compare different management strategies and find the best risk stratification tool for syncope patients.

Conflict of interest: None declared

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